



A116.E1090  
JACC March 9, 2010  
Volume 55, issue 10A



## MYOCARDIAL ISCHEMIA AND INFARCTION

### THE $\beta$ 1 BLOCKER/ $\beta$ 3 AGONIST NEBIVOLOL PROTECTS AGAINST ACUTE MYOCARDIAL INFARCTION IN MICE

ACC Poster Contributions

Georgia World Congress Center, Hall B5

Monday, March 15, 2010, 9:30 a.m.-10:30 a.m.

Session Title: Limitation of Infarct Size

Abstract Category: Myocardial Ischemia/Infarction--Basic

Presentation Number: 1159-306

Authors: Juan Pablo Aragon, Sandeep Patel, Marah Elston, John W. Calvert, David Bennett Grinsfelder, David J. Lefer, Emory University School of Medicine, Atlanta, GA

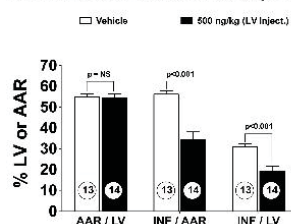
**Background:** Nebivolol (NEB) is a third generation ( $\beta$ 1AR) antagonist and  $\beta$ 3-adrenoceptor ( $\beta$ 3AR) agonist currently used to treat hypertension. Studies indicate that  $\beta$ 3-AR activation promotes eNOS activity and nitric oxide (NO) generation. We hypothesized that acute NEB therapy attenuates the severity of myocardial ischemia-reperfusion (MI-R) injury via  $\beta$ 3-AR stimulation, eNOS activation, and increased NO bioavailability.

**Methods:** Mice were subjected to 45 min of MI in vivo followed by R for 24 hr. NEB (500 ng/kg) or vehicle (VEH) was administered via intracardiac injection at the time of R. At 24 hr of R myocardial area-at-risk (AAR) per left ventricle (LV) and infarct size per area-at-risk (INF/AAR) were evaluated using Evan's Blue and TTC. Serum troponin-I levels were also measured. In separate studies, cardiac tissue and plasma samples were collected from mice treated with NEB or VEH following a single injection to evaluate eNOS phosphorylation (eNOS-P) status as well as plasma nitrite and nitrosothiol levels.

**Results:** NEB significantly reduced INF by 39% ( $p < 0.001$  vs. VEH) and serum troponin-I levels were reduced from  $41 \pm 4$  to  $25 \pm 4$  ng/mL ( $p < 0.05$  vs. VEH). Furthermore, we observed an increase in cardiac eNOS-P of Ser-1177 ( $p < 0.001$  vs. VEH) and a 2-fold increase ( $p < 0.05$  vs. VEH) in plasma nitrite and nitrosothiol levels following NEB treatment.

**Conclusion:** Our results indicate that the protective effects of NEB during acute MI-R are mediated by eNOS activation and increased NO and nitrite bioavailability.

**Nebivolol Reperfusion Therapy and Myocardial Infarct Size**  
45 min of Ischemia and 24 hr of Reperfusion



**Cardiac eNOS Phosphorylation Status**  
Nebivolol (500ng/kg)

